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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,091	12/21/2001	Holly Hogrefe	10070542-01	1719

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

NOTIFICATION DATE	DELIVERY MODE
04/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

IPOPS.LEGAL@agilent.com

Office Action Summary	Application No.	Applicant(s)	
	10/035,091	HOGREFE ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,10-12,14,20,22-24,26,30,31 and 33-51* is/are pending in the application.

4a) Of the above claim(s) *23,24,26,30,31 and 33-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,10-12,14,20,22 and 36-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/1/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 3, 10-12, 14, 20, 22 23, 24, 26, 30, 31, 33-51 are pending and at issue. Applicants arguments presented in the paper of 1/5/2010, are acknowledged and have been considered herein.

Claims 23, 24, 26, 30, 31 and 33-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Upon further consideration it has come to the attention of the examiner that the following rejection should be applied using new art of record.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 10-12, 14, 20, 22, 36, 37, 40, 41, 44, 45, 48-51, are rejected under 35 U.S.C. 103(a) as being unpatentable over Barnes et al. (U.S. Patent No. 5,436,149), Hogreff (U.S. Patent No. 6,183,997) and Sobek et al. (U.S. Patent No. 6,881,559).

For applicants convenience the original rejection is repeated herein:

As previously stated, Barnes teach a number of thermostable DNA polymerase mutants and formulations of the taught DNA polymerases and other thermostable DNA polymerases, which formulation of enzymes are capable of efficiently catalyzing the amplification by PCR of unusually long and faithful DNA products. Barnes specifically

teach a formulation of thermostable DNA polymerases comprising at least one thermostable DNA polymerase lacking 3'-exonuclease activity and at least one thermostable DNA polymerase exhibiting 3'-exonuclease activity, wherein the thermostable DNA polymerase exhibiting 3'-exonuclease activity is a variant of the *Pfu* DNA polymerase wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated.

Sobek et al. teach thermostable mutants of B-type DNA polymerases comprising a Y-GG/A amino acid motif between the N-terminal 3'-5'-exonuclease domain and the C-terminal polymerase domain including Pyrococcus furiosus DNA polymerase, whereas the tyrosine of the Y-GG/A amino acid motif (i.e. Y385H or Y385N or Y385S) is mutated and whereas these mutant DNA polymerases exhibited improved performance in PCR.

Hogrefe (US Patent No. 6,183,997) teaches compositions of non-naturally occurring mixtures of a polymerase enhancing factor protein and multiple DNA polymerases, including Pyrococcus species, JDF3 and KOD DNA polymerases for use in PCR reactions.

One of ordinary skill in the art at the time of filing would have been motivated to use either of the *Pfu* DNA polymerase mutants, Y387H or Y387N or Y387S, taught by Sobek et al. in the formulation taught by Barnes et al. with additional DNA polymerase selected from the group consisting of Pfu, JDF3, KOD and Taq DNA polymerases, as taught by Hogrefe, to catalyze the amplification by PCR of unusually long and faithful DNA products. One would have been further motivated to include in the above

formulation a PCR enhancing factor or an additive, as the purpose of the taught formulation is for PCR and package this formulation as a kit. The motivation for using the *Pfu* DNA polymerase mutants taught by Sobek et al. comes from Barnes who teaches that the thermostable DNA polymerase exhibiting 3'-exonuclease activity of the DNA polymerase formulation is preferably a variant of the *Pfu* DNA polymerase, wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated. The mutants taught by Sobek et al. are such variants of the *Pfu* DNA polymerase, wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated. The reasonable expectation of success is high as both Barnes and Sobek et al. teach a number of thermostable DNA polymerases for use in the taught formulation, and Sobek et al. specifically teach the *Pfu* DNA polymerase mutants, wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated.

Applicants submit that Barnes discloses formulations of thermostable DNA polymerases. The formulations comprise a majority component of a thermostable DNA polymerase lacking 3'-5' exonuclease activity and a minority component of a thermostable DNA polymerase exhibiting 3'-5' exonuclease activity. Applicants submit that In contrast to the position of the Office Applicants submit that *Barnes* is completely silent with regard to use of a *Pfu* DNA polymerase mutant, much less one that has reduced 5'-3' DNA polymerization activity as compared to the wild type *Pfu* DNA polymerase, as recited in the present claims. Applicants submit that the DNA polymerization activity of the "minority component" of the formulations *of Barnes* is

irrelevant to his invention. Applicants submit that to the extent *Barnes* discusses mutant polymerases, it is completely within the context of mutant *Taq* DNA polymerases, and is completely restricted to thermostability and abolishment of 3'-5' exonuclease activity. *Barnes* makes no reference to any mutant polymerase having reduced 5'-3' DNA polymerization activity as compared to the wild type DNA polymerase from which it is derived.

Applicants submit that in the present situation, *Barnes* does not disclose or suggest an enzyme mixture comprising two enzymes, wherein one of the enzymes is a mutant *Pfu* DNA polymerase that possesses 3'-5' exonuclease activity and reduced 5'-3' DNA polymerization activity as compared to the wild type *Pfu* DNA polymerase.

Applicants submit that *Sobek* is focused on providing DNA polymerases that are suitable for use in PCR as the sole polymerase in the reaction and *Sobek* does not disclose the use of its DNA polymerase mutants in an enzyme mixture and provides no motivation to use them in a mixture.

Applicants submit that the disclosure *of Hogrefe* does not provide for an enzyme mixture that includes a *Pfu* mutant according to the present claims. Accordingly, regardless of the teachings *of Hogrefe* relating to a polymerase enhancing factor, *Hogrefe* does not provide the features of the presently claimed invention that are lacking from the combined teachings *of Barnes* and *Sobek*.

Applicants submit that because the combination *of Barnes, Sobek,* and *Hogrefe* does not disclose or suggest all of the elements of the pending claims, and does not

provide any motivation to combine the respective teachings, Applicants submit that the combination *of Barnes, Sobek,* and *Hogrefe* fails to support *prima-facie* case of obviousness against present claims 1, 3, 10-12, 14, 20, 22, 36, 37, 40, 41, 44, 45, and 48-51.

Applicant's complete argument is acknowledged and has been carefully considered, however, is not found persuasive for the reasons originally presented and repeated herein.

Initially in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

It appears that applicants traversal of the rejection is on the basis that applicants submit that *Barnes* is completely silent with regard to use of a *Pfu* DNA polymerase mutant, much less one that has reduced 5'-3' DNA polymerization activity as compared to the wild type *Pfu* DNA polymerase, as recited in the present claims. Applicants submit that to the extent *Barnes* discusses mutant polymerases, it is completely within the context of mutant *Taq* DNA polymerases, and is completely restricted to thermostability and abolishment of 3'-5' exonuclease activity. *Barnes* makes no reference to any mutant polymerase having reduced 5'-3' DNA polymerization activity as compared to the wild type DNA polymerase from which it is derived.

In response to this argument applicants attention is directed to issued claim 8 of Barnes et al. which recites "A formulation of thermostable DNA polymerases as set forth in claim 6 wherein the at least one thermostable DNA polymerase exhibiting 3'-exonuclease activity is selected from the group consisting of Pfu polymerase from *Pyroccus furiosus*, the Vent DNA polymerase from *Thermococcus litoralis*, a variant of the *Pfu* DNA polymerase wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated, or a variant of the Vent DNA polymerase wherein the DNA polymerase activity of said Vent DNA polymerase has been diminished or inactivated.

Thus applicants assertion that Barnes et al. makes no reference to any mutant polymerase having reduced 5'-3' DNA polymerization activity is unclear on the basis that the reduced DNA polymerase activity referred to above is clearly 5'-3' DNA polymerization activity as no other type of polymerization activity exists, only 5'-3' DNA polymerization activity.

Thus as this is the only basis of applicants traversal, applicants traversal is not found persuasive. As previously stated, one of ordinary skill in the art at the time of filing would have been motivated to use either of the *Pfu* DNA polymerase mutants, Y387H or Y387N or Y387S, taught by Sobek et al. in the formulation taught by Barnes et al. with additional DNA polymerase selected from the group consisting of Pfu, JDF3, KOD and Taq DNA polymerases, as taught by Hogrefe, to catalyze the amplification by PCR of unusually long and faithful DNA products. One would have been further motivated to include in the above formulation a PCR enhancing factor or an additive, as

the purpose of the taught formulation is for PCR and package this formulation as a kit. The motivation for using the *Pfu* DNA polymerase mutants taught by Sobek et al. comes from Barnes who teaches that the thermostable DNA polymerase exhibiting 3'-exonuclease activity of the DNA polymerase formulation is preferably a variant of the *Pfu* DNA polymerase, wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated. The mutants taught by Sobek et al. are such variants of the *Pfu* DNA polymerase, wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated. The reasonable expectation of success is high as both Barnes and Sobek et al. teach a number of thermostable DNA polymerases for use in the taught formulation, and Sobek et al. specifically teach the *Pfu* DNA polymerase mutants, wherein the DNA polymerase activity of said *Pfu* DNA polymerase has been diminished or inactivated.

Thus claims 1-3, 7, 8, 10-14, 18, 20-22 are made obvious over Barnes et al., Hogrefe and Sobek et al.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 10-12, 14, 20, 22 and 36-51 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1, 2, 5-8, 22, 27, 31, 33, 40-44, of copending Application No. 10/702,400. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claimed enzyme mixtures of the instant application, comprising a first enzyme and a second enzyme wherein said first enzyme comprises a DNA polymerization activity and said second enzyme is a mutant Pfu DNA polymerase having a mutation at an amino acid position selected from the group consisting of D405, Y410, T542, K593, Y595, Y385, Y387, and G388 and those further limited claims dependent thereon are anticipated by and thus obvious over the corresponding claims of copending Application No. 10/702,400, drawn to a blend of two or more DNA polymerases comprising at least two fusion polypeptide DNA polymerases, each having a proofreading activity wherein one of said polypeptide DNA polymerase has a mutation at an amino acid position of Y387 and those further limited claims dependent thereon.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants request to keep this rejection in abeyance until the time of identification of otherwise allowable subject matter is acknowledged.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
4/20/2010

/Richard G Hutson/
Primary Examiner, Art Unit 1652